

PATENT

Case 5400/2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

S. BERTENSHAW ET AL

SERIAL NO.: 08/425,022

FILED: April 19, 1995

GROUP ART UNIT: 120

EXAMINER: DENTZ

DATE: April 3, 1997

TITLE: SUBSTITUTED FURANS AND FURANONES
FOR THE TREATMENT OF INFLAMMATION

DECLARATION UNDER 37 C.F.R. §1.132

The Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

I, Richard B. Silverman, Ph.D., declare that:

1. I received a Bachelor of Science Degree in Chemistry from Pennsylvania State University, in 1968; and received a Ph.D. in Chemistry from Harvard University in 1974;

2. Since 1976, I have been employed as a faculty member of the Chemistry Department at Northwestern University, Evanston, Illinois, and that currently I hold the position of Arthur Andersen Teaching and Research Professor of Chemistry and of Biochemistry, Molecular Biology and Cell Biology, with responsibility for scientists carrying out research in medicinal chemistry;

3. I am the principal author or co-author of approximately 150 publications and books, with several publications on organic

chemistry synthesis methods, including the synthesis of dihydrofuranone compounds;

4. In my professional capacities, I closely and carefully follow the scientific literature regarding organic chemistry and specifically synthetic methods;

5. As a professor of chemistry at Northwestern University, with teaching responsibilities for undergraduate and graduate students, I am aware of what constitutes ordinary skill and knowledge in the art of heterocyclic chemistry, including as it relates to tautomers. In this art it is well known and accepted that:

a. carbonyl-enol tautomerism exists where an enol (vinyl alcohol) form exists in equilibrium with one or more carbonyl forms;

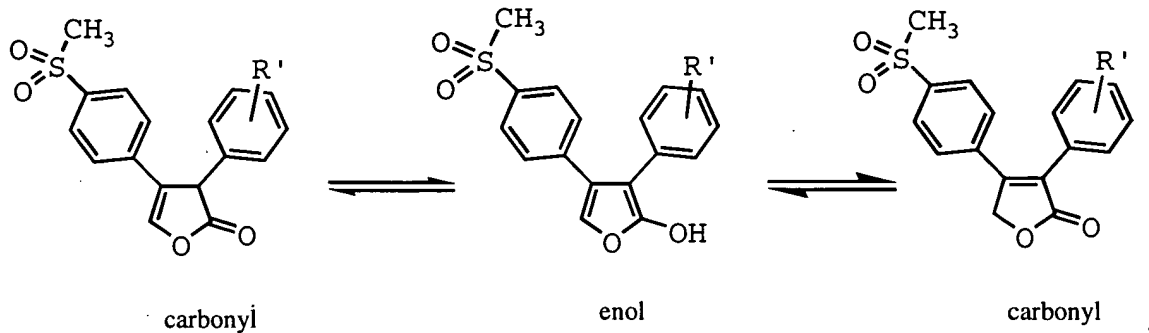
b. the carbonyl-enol tautomeric forms are interconvertable by transfer of a proton;

c. although one tautomeric form may predominate, in solution phase the carbonyl-enol tautomeric forms co-exist;

d. the carbonyl-enol tautomeric equilibrium is greatly affected by phase, solvent, concentration, pH, temperature and the presence of substituents (including those producing inductive, resonance, hydrogen bond-stabilizing or steric effects); and

e. a depiction of one carbonyl-enol tautomeric form embodies all carbonyl-enol tautomeric forms;

6. The structures shown below are tautomers of each other



7. I have reviewed U.S. Patent Application Serial No. 08/004,822. The application describes hydroxyl-substituted 3,4-diarylfurans (pages 2-3);

8. Based on my analysis, I believe one of ordinary skill in this art, including as it relates to tautomers, would understand that U.S. Patent Application No. 08/004,822 describes both the 3,4-diaryl-2-hydroxyfuran enol and carbonyl forms;

I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Respectfully submitted

4/7/97
Date

Richard B. Silverman
Richard B. Silverman, Ph.D.